Haemodialysis with Charcoal Haemoperfusion

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Summary

An activated charcoal haemoperfusion device containing 300 g acrylic hydrogel coated activated charcoal, was combined with haemodialysis, on six occasions in each of two patients, for a 2-hour portion of a routine 5-hour dialysis schedule. Blood pressure changes with combined treatment were minimised by using a low priming volume dialysis filter. Plasma clearance of both creatinine and urate were increased during the combined haemodialysis-haemoperfusion period. During the two hours of the combined treatment period in one patient creatinine removal amounted to 70% and urate removal to 50% of that obtained during a 5-hour haemodialysis. No significant additional urea or phosphate removal occurred. Changes in middle molecular weight substances with combined treatment were slightly greater than changes occurring with dialysis alone.

Haemodialysis alone did not result in a terminal platelet fall, but combined treatment resulted in a terminal 20-30% platelet reduction, despite unchanged platelet counts at the end of the 2-hour haemoperfusion period.

This preliminary study suggests that combined haemodialysis-haemoperfusion, is worthy of further scrutiny.

Introduction

Although activated charcoal as a decontaminant sorbent has been used in industry and clinical toxicology for many years, only since the report of Yatzidis (1964) has attention been focused on haemoperfusion through activated charcoal particles, as a means of directly removing many endogenous and exogenous toxins from blood. Initial problems with platelet depletion (Dunna & Kolff, 1965) and small particle embolisation (Hagstam et al, 1966) associated with uncoated and poorly washed activated carbons, have been largely overcome with suitable polymer coatings (Chang, 1966; Andrade et al, 1972; Winchester et al, 1974; Gazzard et al, 1974; Vale et al, 1975).
Since activated charcoal haemoperfusion is known to remove creatinine, uric acid, guanidines, organic acids (Yatzidis, 1964) amino acids (Chang et al. 1970) and middle molecular weight substances (Chang et al. 1974) but not to remove urea and electrolytes, we decided to investigate the effect of haemoperfusion combined with routine haemodialysis in stable uraemic subjects. The device used was a column containing 300 g acrylic hydrogel coated activated charcoal initially developed for the treatment of severe drug overdosage (Fennimore & Munro, 1975).

MATERIALS AND METHODS

In this unit the haemodialysis schedule is five hours haemodialysis thrice weekly. Two patients stabilised on this regime gave their informed consent for the investigation.

In the first patient, normally treated with a Travenol ‘145’ twin coil, using an RSP machine, six standard haemodialyses were studied. In a further six dialyses the activated charcoal haemoperfusion device was inserted into the dialysis circuit for a period of two hours. After this combined two hour period blood in the haemoperfusion device was returned to the patient and dialysis thereafter continued for a further three hours. Throughout the study blood flow rates were maintained at 300-330 ml/min and dialysate flow rates 200 ml/min. In three combined haemodialyses/haemoperfusions the charcoal device was placed distal to the dialysis coil and in three the device was placed proximal to the coil.

In the second patient six standard dialyses using a hollow fibre artificial kidney (Cordis Dow Mark IV) were studied. Thereafter the charcoal device was combined with dialysis in the same manner as described above in six further dialyses. Blood flow rates were maintained at 300 ml/min and dialysate flow rates at 500 ml/min using a dialysate proportionating system.

Blood was withdrawn before and after standard dialysis and before and after combined haemodialysis and haemoperfusion for platelet counts, leucocyte counts, coagulation studies, and medium molecular weight substance estimation (Dallaglio et al, 1972) as well as measurements of plasma creatinine, urate, urea and phosphate. Timed samples of blood were also taken during dialysis and during combined haemodialysis-haemoperfusion for platelet, leucocyte, creatinine, uric acid, urea and phosphate determinations. Determinations of dialysate volume and creatinine, uric acid, urea and phosphate were made.

Solute clearances were calculated in the normal fashion, and total solute removal during dialysis and during combined dialysis/haemoperfusion was derived from calculation of the area between inlet-outlet concentration versus time curve as reported previously (Winchester et al, 1975).

The effect of combined dialysis/haemoperfusion on blood pressure was carefully monitored.

At the cessation of haemoperfusion the device was opened and visually inspected for thrombus formation.
RESULTS

Siting of the charcoal device proximal or distal to the haemodialysis filter was not associated with differences in additional solute removal and for simplicity the results are combined.

For Patient 1 the plasma clearances mean ml/min ± S D of creatinine and urate are depicted in Figures 1 and 2 respectively. No significant increase in urea or phosphate clearance was observed with combined haemoperfusion-haemodialysis. Both creatinine and urate clearance were significantly increased during the combined treatment period, by about 100% and 50% respectively.

![Figure 1](image1.png)

Figure 1. Creatinine clearance (ml/min) for Travenol dialysis, haemoperfusion and combined haemodialysis-haemoperfusion in patient 1. All points M ± S D of six treatments.

![Figure 2](image2.png)

Figure 2. Urate clearance (ml/min) for Travenol dialysis, haemoperfusion and combined haemodialysis-haemoperfusion in patient 1. All points M ± S D of six treatments.
TABLE I. Total solute removal of creatinine, urea and urate (g) obtained with dialysis alone, haemoperfusion and combined haemodialysis-haemoperfusion (M ± S D of six investigations).

<table>
<thead>
<tr>
<th></th>
<th>PATIENT 1</th>
<th></th>
<th></th>
<th>PATIENT 2</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Total Solute Removal</td>
<td>5 hr. dialysis alone</td>
<td>2 hr. haemoperfusion</td>
<td>2 hr. combined dial/haemo.</td>
<td>5 hr. dialysis alone</td>
<td>2 hr. haemoperfusion</td>
</tr>
<tr>
<td>Urea (g)</td>
<td>27.7 ± 3.8</td>
<td>–</td>
<td>15.5 ± 3.2*</td>
<td>9.8 ± 3.6</td>
<td>–</td>
<td>13.5 ± 3.6*</td>
</tr>
<tr>
<td>Creatinine (g)</td>
<td>2.0 ± 0.14</td>
<td>0.9 ± 0.16</td>
<td>1.4 ± 0.3*</td>
<td>2.7 ± 0.34</td>
<td>0.6 ± 0.23</td>
<td>1.2 ± 0.2</td>
</tr>
<tr>
<td>Urate (g)</td>
<td>1.5 ± 0.34</td>
<td>0.4 ± 0.1</td>
<td>0.9 ± 0.1*</td>
<td>1.5 ± 0.3</td>
<td>0.2 ± 0.03</td>
<td>0.6 ± 0.1*</td>
</tr>
</tbody>
</table>

* significantly less than 5 hour haemodialysis alone (p < 0.005)

In Patient 2 similar results were obtained, although the creatinine and urate clearances with the Cordis Dow device were higher than in Patient 1, while the creatinine and urate clearances with the haemoperfusion device were lower than in Patient 1.

Total solute removal of urea, creatinine and urate are presented in Table I. In Patient 1 with the two hour combined system creatinine removal was approximately 70% and urate removal was approximately 55% of that removed in a standard 5-hour haemodialysis. In Patient 2, however, lower solute removal of creatinine and uric acid was observed.

With the analytical techniques used a slight increase in middle molecular weight substance removal was obtained by the addition of haemoperfusion to standard dialysis.

Transient leucopenia was observed during combined treatment, although this was not significantly different from that observed during dialysis alone.

The change in platelet counts observed during standard dialysis and combined dialysis-haemoperfusion are depicted in Figure 3. Although there were moderate changes in platelet counts at the initiation of haemoperfusion at the end of the 2-hour period falls in platelet counts across the haemoperfusion device were minimal. However, it was noted that following combined-haemoperfusion, at the cessation of the dialysis period, platelet counts were 20-30% lower than at the beginning of dialysis.

529
Figure 3. Changes in platelet counts (%) during combined haemodialysis-haemoperfusion and dialysis alone. Circuit A – haemoperfusion device distal to dialysis filter. Circuit B – haemoperfusion device proximal to dialysis filter.

Blood pressure changes were most marked during combined (Travenol 145) haemoperfusion periods (total blood priming volume approximately 650 ml) while only minimal changes occurred during combined (Cordis Dow) haemoperfusion periods (total blood priming volume 450 ml).

No thrombus formation was observed in the charcoal haemoperfusion device, except for very occasional fibrin strands over the inlet filters.

**DISCUSSION**

The adsorptive properties of activated charcoal for uraemic toxins are increasingly being used in the treatment of uraemia in the form of oral activated charcoal (Friedman et al, 1975), as a constituent of a dialysate regeneration system (Gordon et al, 1970) or wearable artificial kidney (Jacobsen, 1974), and in haemoperfusion devices (Chang, 1966). Chang et al (1970) initially reported the use of activated charcoal haemoperfusion in uraemic patients with high urine volumes, or substitution of one or more dialyses with haemoperfusion, since the major disadvantage of haemoperfusion alone was inability to remove fluid or correct electrolyte abnormalities. More recently however, Chang et al (1975) have reported the use of combined haemoperfusion-haemodialysis or ultrafiltration in the maintenance of regular dialysis patients, although no long-term therapy with the system was discussed.
The haemoperfusion device used in this study has not been previously used in the treatment of uraemia, although it has been used successfully in the treatment of severe drug overdosage (Vale et al, 1975) and in the treatment of fulminant hepatic failure (Gazzard et al, 1974), where profound thrombocytopenia, a distinct problem with initial usage of uncoated charcoal (Dunea & Kolff, 1965), has rarely been encountered.

We have demonstrated in this study that the device is not associated with large falls in platelet numbers, but may be associated with a 20-30% platelet fall at the end of the dialysis, three hours after the combined haemoperfusion-haemodialysis period, possibly due to an alteration in platelet reactivity.

With the system used in this study clearance of both urate and creatinine were significantly increased during the combined treatment period, and resulted in significantly increased total solute removal of urate and creatinine. The lower urate and creatinine removal obtained in Patient 2, cannot be fully explained, although several factors such as inter-batch variation or different flow characteristics resulting from the hollow fibre artificial kidney in combination, may explain the results.

Certainly the concept of combination charcoal haemoperfusion with a hollow fibre device as an ultrafiltrator, is attractive, in view of the lower priming volume obtained and straightforward use when compared to conventional dialysis devices.

An extension of the period of combined treatment for example to three hours, should increase total solute removal and is worthy of further investigation.

Although we were unable to demonstrate a large increase in middle molecular weight substance removal, the method used for estimation of middle molecules was unable to separate peptides into subpeaks such as those obtained on gradient-elution chromatography (Furst et al, 1974). It has recently been reported that peptide subpeaks are significantly decreased by dialysis or a sorbent based dialysate regeneration system (Gordon et al, 1975).

In this pilot study we have shown that combined haemoperfusion-haemodialysis can increase the efficiency of dialysis and is not associated with unacceptable platelet depletion.

ACKNOWLEDGMENTS

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References


Jacobsen, S C (1974) Medical Instrumentation, 8, 138


Open Discussion

SHALDON (Montpellier)  Could you tell us the extracorporeal blood volume in your charcoal device? Are you sure that this approach towards reduction in dialysis is sound?

WINCHESTER  Reducing dialysis time is more comfortable for our patients and using this dialyser combination middle molecules and other substances may be removed. In fact one can remove certain polypeptide fractions of the middle molecules. The extra corporeal volume in the ‘145’ charcoal device is about 600 ml; we noticed that the blood pressure using the combined ‘145’ and charcoal device did fall occasionally.

CAMBI (Parma)  What are the metabolic advantages of charcoal haemoperfusion? The cost is also very high.

WINCHESTER  We do not know at present. The method is simple and may find some acceptability.